Remarks

A. Status of the Claims

Claims 1-9, 11 and 12 were pending in the case at the time the Action was mailed. Claims 1, 2, 11 and 12 have been amended. Claims 3-5 have been cancelled without prejudice or disclaimer. New claims 13-28 have been added. Support for the amendments and the new claims can be found generally throughout the specification and the claims as originally filed, as explained below. No new matter is added by virtue of the amendments or the new claims. Claims 1, 2, 6-9 and 11-28 are pending.

B. The Amended and New Claims Are Properly Supported

1. Claim Amendments and Support Therefore

Present claims 1 and 2 have been revised to indicate that the recited powders have different granular sizes and shapes. Non-limiting support for this recitation may be found in the specification at paras. [0003] and [0004]. Claims 1 and 2 have also been amended to indicate that the method "does not comprise addition of a loss-compensatory overage amount of Doxylamine Succinate." Non-limiting support for this recitation may be found at para. [0004] and Example 2. Claims 11 and 12 have been amended to more clearly state that the unitary dosage forms comprise or consist of equal parts of active ingredients.

2. New Claims 13-28 And Support Therefore

Support for each of new claims 13-28 may be found in the specification and/or the originally-filed claims in at least the following manners: claims 13 and 21 (paras. [0016] and [0018] and Example 2); claims 14 and 22-24 (para. [0004] and Example 2 and originally filed claims 1 and 2); claims 15-20 (paras. [0016] and [0033] and originally-filed claims 6-12); claims 25-28 (paras. [0014], [0018] and [0028]-[0029]).

C. The Indefiniteness Rejection Is Overcome

Claims 4 and 5 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In essence, the Examiner contends that it is unclear which active ingredient(s) is used in which step(s).

Applicant respectfully traverses, as a skilled artisan would understand the metes and bounds of this phrase when read in light of the specification, as permitted. *See* MPEP § 2173.05(a). However, in order to advance prosecution and secure prompt allowance in this case, claims 4 and 5 are cancelled without prejudice or disclaimer. The rejection is therefore moot.

D. The Obviousness Rejection Is Overcome

Claims 1-9, 11 and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chen (U.S. Patent 5,260,069) in view of Chu *et al.* (U.S. Patent 6,419,954), Bishai *et al.*, (*Today's Therapeutic Trends*, Princeton Junction, NJ, 17:167-179, 1999) and what the Examiner characterizes as "the acknowledged prior art." Applicant respectfully disagrees with the rejection and, in particular, the arguments presented at pp 3-6 of the Action which substantially rely on Applicant's "acknowledged prior art." The present claims are not obvious for at least the following reasons.

1. Overview of the Argument

The language of the specification characterized as "acknowledged prior art" in the Action is not prior art under any statute, nor is it prior art by way of any admission on the part of Applicant. In particular, the previously unknown reasons for the lack of uniform dry mixing of powdered Pyridoxine HCl and Doxylamine Succinate, and the solutions found by the inventors regarding this problem may not be characterized as prior art as they concern the inventors' own work. Moreover, this work was not made known publicly prior to the filing of the application.

Without the availability of the inventors' own work as prior art, the obviousness rejection necessarily falls.

Should the Examiner disagree with Applicant's showing that the inventors' own work is not prior art and insist on relying on such to support the obviousness rejection, Applicant provides declaratory evidence of unexpected results that rebuts any *prima facie* showing of obviousness. Moreover, the unexpected results are commensurate with the scope of the claims, as will be explained.

Finally, should the Examiner agree that the "acknowledged prior art" is not prior art, any attempt by the Examiner to rely on Chen, Chu and Bishai alone to assert obviousness fails because not only is every element of the claimed invention not taught by any combination of these references, nor is the invention as a whole rendered obvious in view of these references, but there is also no apparent reason to combine any of this information to arrive at the subject matter of the present claims.

Each of these points will now be addressed in the following sections.

2. Information in the Specification Relied Upon In the Action As "Acknowledged Prior Art" is Not Prior Art for Purposes of An Obviousness Rejection and Thus, the Obviousness Rejection Should Be Withdrawn

Several pieces of information in the specification are characterized in the Action as "acknowledged prior art," including the following:

> The Applicant acknowledges that doxylamine succinate and pyridoxine HCL are obtained in the form of powders having different granular sizes which makes it very difficult to

uniformly mix them in dry state long with require excipients (Paragraph 0003). It is acknowledged that the loss of pyridoxine HCL during processing is due to the small size of and possible electrostatic charge of the Pyrdoxine HCL particles and that simply account of the loss by using increased amounts of Pyridoxine HCl does not result in consistant results (Paragraph 0004).

Action, pp 3-4;

the prior art discloses the combination of doxylamine succinate and pyridoxine HCl and that pyridoxine HCL and doxylamine succinate are provided in different granular sizes.

Id. at p 4; and

Contrary to the Applicant's arguments, it is acknowledged by Applicant that pyridoxine HCl and doxylamine succinate are in the form of powders having different granular sizes and that said lack of uniformity creates problems in processing in terms of loss of pyridoxine HCl.

Id. at p 5. The Examiner relies on this "acknowledged prior art" to support the obviousness rejection. Action, pp 4-5. However, this "acknowledged prior art" is ***not*** prior art for purposes of an obviousness rejection. Without this information, the obviousness rejection necessarily falls.

a. An inventor's own, unpublished work cannot serve as prior art

The MPEP differentiates between two types of admissions made by an applicant either in the specification or during prosecution that regard work performed before the date of an invention: admissions that identify work that is of another, and admission that identify work that is of the same inventive entity as the application in question. MPEP § 2129. Work that is of another "can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories

of 35 U.S.C. 102." *Id.* By contrast, "***even if labeled as 'prior art,'*** the work of the same inventive entity may not be considered prior art against the claims unless it falls under one of the statutory categories." *Id.* (boldface emphasis added; underlined emphasis in original). "Consequently, the examiner must determine whether the subject matter identified as 'prior art' is applicant's own work, or the work of another." *Id.*

Applicants may submit evidence that information in the specification or submitted during prosecution that *appears* to be "prior art" is actually the inventors' own work. *See, e.g., Riverwood Int'l Corp. v. R. A. Jones & Co., Inc.*, 324 F.3d 1346, 1351 (Fed. Cir. 2003) (applicant offered evidence that information cited in an Information Disclosure Statement was not the work of another but of the inventor); *see also In re Ehrreich*, 590 F.2d 902, 909-910 (CCPA 1979) (applicant explained that reason for Jepson claim preamble was to distinguish claim from inventor's co-pending application and not work of another). Evidence that the allegedly "acknowledged prior art" is not "prior art" for the purposes of an obviousness rejection will now be presented.

b. The "acknowledged prior art" is the inventors' own work

Applicant attaches the Shulman Declaration (Appendix 1) which confirms that the "acknowledged prior art" is actually the inventors' own work: thus, this information is not "prior art" for the purposes of the present obviousness rejection. Statements made in the specification, such as those found in paragraphs [0003] and [0004], result from observations, testing and experiments made by the same inventive entity as that of the patent application. Shulman Declaration, paras. 24-48. Thus, although these statements are made in the "Background of the Invention" section of the application, such statements are not "prior art" for purposes of an obviousness rejection. In the same way, information provided in Example 1 of the specification,

titled "Prior Art," is not "prior art" for the purposes of the present obviousness rejection as that information was also obtained by the same inventive entity. Shulman Declaration, para. 17.

For example, Mr. Shulman explains that the powders of Pyridoxine HCl and Doxylamine Succinate surprisingly proved impossible to dry mix with a satisfying content uniformity, even after many attempts with classical techniques of dry blending, such as size reduction and various blending times. Declaration, paras. 24-33. Paragraph [0003] of the present specification, for example, discusses some of these difficulties.

In addition, the microstructure of the powders was studied to investigate the source of the active ingredient dry blending problem: microscopic analysis is a step not commonly performed in the industry, particularly since it is a tedious and expensive method. Declaration, paras. 34-37 and 47. It was not until both powders were looked at under a microscope that the inventors determined the reason for the impossible uniform mixing. Declaration, para. 47. They observed that Pyridoxine HCl has a granular hard crystalline structure while Doxylamine succinate has a rod shaped, waxy structure. Declaration, paras. 39-46 and the accompanying figures. One problem that therefore had to be overcome, they determined, regarded how to uniformly mix a granular powder with a wax. Declaration, paras. 34-48. Paragraph [0004] of the present specification, for example, speaks to this information.

Finally, the Declaration confirms that information presented in at least paragraphs [0003] and [0004] and Example 1 of the specification was not publicly disclosed more than one year prior to the invention date. Declaration, paras. 61 and 65. Thus, none of this information qualifies as statutory prior art. As such, this information is work of the present inventors and is not part of any prior art applicable to any obviousness rejection of the present claims.

c. A statement in the specification regarding the purpose behind an invention is not prior art

Observations made by the present inventors defined the problem that they then set out to solve. Accordingly, the specification states the following: "Thus, there is a need for a method of manufacturing Diclectin® or other similar powderous multi-ingredient medicaments which alleviate ingredient losses during manufacturing and provides superior content uniformity results when compared to known methods." Specification, para. [0006]. Applicant further notes that this statement, too, may not be considered for any prior art purposes with respect to an obviousness rejection. The Federal Circuit made it clear that "a patent applicant's statement of the purpose of the work is not prior art." *In re Dow*, 837 F.2d. 469 (Fed. Cir. 1988). Thus, an obviousness rejection may not be supported by any such statement in the specification.

d. Without the availability of the "acknowledged prior art," the obviousness rejection fails

The discussion above establishes that Applicant has set forth a "credible explanation" demonstrating that certain statements in the specification stem from the inventors' own work and not any work of the prior art. MPEP § 2129. Accordingly, each piece of information characterized in the Action as "acknowledged prior art" is therefore *not* prior art for purposes of an obviousness rejection. Without this information, the reasoning behind the obviousness rejection falls apart. Each aspect of the reasoning appears to have within it an intertwining of the teachings of Chu, Chen, Bishai *and* the "acknowledged prior art." No aspect of the obviousness rejection relies upon only Chu, Chen and Bishai, by themselves.* Instead, the rejection is said to be supported by Chu, Chen, Bishai *and* "acknowledged prior art," the latter of which is actually not prior art, as explained above. Without the "acknowledged prior art," the obviousness rejection is improperly supported. This, then, presents at least one reason why the obviousness rejection must be withdrawn.

* Applicant addresses the possibility of a rejection based on a combination of Chu, Chen and Bishai below.

3. The Surprising and Unexpected Results Observed By the Inventors Overcome Any *Prima Facie* Case of Obviousness

The presently claimed invention provides surprising and unexpected results as to alleviation of ingredient loss during manufacturing of pharmaceutical dosage forms comprising Pyridoxine HCl and Doxylamine Succinate as active ingredients. The presently claimed invention also results in beneficial content uniformity of such active ingredients.

Firstly, unexpected results associated with the presently claimed methods are clearly apparent from the comparison between Example 1 and Example 2, which were conducted using Pyridoxine HCl and Doxylamine Succinate as powdered active ingredients having different granular sizes and shapes. *See also* paras. [0003], [0004] and [0020]. Example 1 shows, for example, why an overage of Pyridoxine HCl would presumably be necessary in order to account for product loss as well as to achieve content uniformity: Pyridoxine HCl loss averaged 17.8% over the course of five dry blending experiments. By contrast, Example 2 shows that the roller compaction method of the presently claimed invention achieves both a dramatic minimization of Pyridoxine HCl loss (see paragraphs [0027] and [0028]) and a realization of content uniformity of the granular blend in terms of active ingredients (*see, e.g.*, paragraph [0029]).

Secondly, these unexpected results are further explained in the Shulman Declaration (Appendix 1). For example, Mr. Shulman explains that there was no expectation or connection placed on the roller compacting method having any effect on the relative loss of Pyridoxine HCl in the manufacturing process of Doxylamine Succinate and Pyridoxine HCl containing dosage forms. Declaration, paras. 49-51; *see also* paras. 62 and 63. He further explains that for this reason, when first introducing roller compaction into the manufacturing process, the previous standard of about 10% overage of Pyridoxine HCl was employed. Declaration, paras. 16 and 50. After studying the resulting tablets, this overage was determined to be unexpectedly unnecessary.

Declaration, para. 51. It was only then that the beneficial use of roller compaction for alleviating Pyridoxine HCl loss was uncovered. *Id.* As Mr. Shulman explains, such a result was not part of the predictable uses of this apparatus for persons knowledgeable of roller compacting techniques, such as the present inventors, let alone for any other person of ordinary skill in the art. Declaration, paras. 50, 51, 62, 63 and 66.

As noted in the specification, roller compaction was also found to provide active ingredient content uniformity in the resulting dosage forms comprising Pyridoxine HCl and Doxylamine Succinate. Specification, paras. [0014] and [0018]. Mr. Shulman explains that he could not have predicted, despite his knowledge of the roller compacting technique, that the content uniformity of the resulting granules would satisfy the strict FDA requirements with a Relative Standard Deviation of than 5%. Declaration, paras. 52-53.

The unexpected results stemming from the use of a roller compactor are commensurate with the scope of the claims in accordance with MPEP § 716.02(d). For example, both independent claims 1 and 2 refer to methods that "[do] not comprise addition of a loss-compensatory overage amount of Pyridoxine HCl." Both independent claims 23 and 24 refer to methods "wherein the unitary dosage forms do not contain a loss-compensatory overage amount of Pyridoxine HCl." Moreover, new dependent claims 25-28 each recite subject matter pertaining to achieving content uniformity in terms of active ingredients using the methods of claims 1, 2, 23 and 24. Indeed, since all dependent claims depend from one of claims 1, 2, 23 and 24, all of the present claims are properly commensurate in scope with the presently claimed invention.

It appears that the Examiner believes that the unexpected results are necessarily tied to the mesh size of 16 employed in Example 2 of the specification. *See, e.g.*, Action, p 5.

Applicant respectfully disagrees. As discussed above, the unexpected results do not depend on a particular mesh size. In addition, the examples in the Examples section are merely demonstrations of methods of the present invention. *See* para. [0021]. Mr. Shulman also states that a mesh size of 16 is not the only mesh size that may be employed in the claimed methods: for example, a mesh size of 20 would also work. Declaration, para. 54. Thus, the independent claims do not need to be restricted to a mesh size of 16 to be commensurate in scope with the unexpected results discussed above.

Accordingly, even if a *prima facie* case of obviousness has been established by the Examiner, which Applicant does not concede, the obviousness rejection cannot stand in view of these secondary considerations. *See* MPEP § 2141; *see also In re Pravin*, 54 F.3d 746, 750 (Fed. Cir. 1995) (a showing that the invention exhibits a "superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected" is one way to rebut a *prima facie* case of obviousness); *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739 (2007) ("A rationale to support a conclusion that a claim would have been obvious is that... [in part,] the combination would have yielded nothing more than predictable results to one of ordinary skill in the art.").

4. Any Combination of Chu, Chen and Bishai Relied Upon In the Action Does Not Support A *Prima Facie* Case of Obviousness

In the present Action, it is asserted that that a combination of Chu, Chen, Bishai and the "acknowledged prior art" renders claims 1, 2 and 9-11 obvious. As explained above, the "acknowledged prior art" is actually the inventors' own work, and is therefore unavailable as prior art in the context of an obviousness rejection. If the Examiner accepts Applicant's explanation regarding the "acknowledged prior art" but maintains an obviousness rejection over

the combined teachings of Chu, Chen and Bishai alone, Applicant provides the following arguments to show that such a rejection would be improper.

Citing the *KSR* decision, section 2143.02 of the MPEP states,

> A rationale to support a conclusion that a claim would have been obvious is that ***all the claimed elements were known in the prior art*** and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions....

KSR also states that

> Section 103 forbids issuance of a patent when 'the differences between the subject matter sought to be patented and the prior art are such that ***the subject matter as a whole*** would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

127 S.Ct. 1734. Viewing the subject matter of the presently claimed invention as a whole in light of Chen, Chu and Bishai (collectively, "the prior art") does not lead a person of ordinary skill in the art to a conclusion of obviousness under § 103.

At a minimum, the prior art fails to disclose a manufacturing method for producing pharmaceutical dosage forms comprising Pyridoxine HCl and Doxylamine Succinate as active ingredients, "wherein the method does not comprise addition of a loss-compensatory overage amount of Pyridoxine HCl" as recited in claims 1 and 2 or "wherein the unitary dosage forms do not contain a loss-compensatory overage amount of Pyridoxine HCl" as recited in claims 23 and 24 as well as claims 14 and 22. Regarding claims 25-28 in particular, none of the references speak to "wherein the similar sized granules present content uniformity in terms of active ingredients." Indeed, none of these references discuss any problem regarding an overage need for Pyridoxine HCl in a pharmaceutical dosage form that comprises Pyridoxine HCl and Doxylamine Succinate as active ingredients, nor any content uniformity problem regarding a

pharmaceutical dosage form comprising Pyridoxine HCl and Doxylamine Succinate as active ingredients, much less use of roller compaction to specifically address these problems.

For at least these reasons, the claimed invention, as a whole or in its particulars, is neither taught nor suggested in the combined teachings of the prior art. Moreover, since these problems were not even discussed in any of these references, there is no apparent reason why a skilled artisan would combine these references to arrive at the presently claimed invention. *See KSR*, 127 S. Ct. at 1741 (there should be an "explicit" analysis regarding "whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue."). Applicant further notes that the surprising and unexpected results discussed above are also surprising and unexpected in view of Chu, Chen and Bishai alone. As such, any obviousness rejection based only on Chen, Chu and Bishai would be improper.

E. Conclusion

In view of the foregoing, it is respectfully submitted that each of the pending claims is in condition for allowance, and a Notice of Allowance is earnestly solicited. The Examiner is invited to contact the undersigned attorney at (512) 536-3015 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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Appendix 1